REMARKS

This Amendment is submitted in response to the February 25, 2008 Final Office Action issued by the United States Patent and Trademark Office. Claims 18-21 have been canceled hereinabove without prejudice and new claims 22-25 have been submitted. Support for new claims 22-25 may be found throughout the specification, including, for example, pages 30-35. Accordingly, no new matter is introduced by new claims 22-25. Upon entry of this Amendment new claims 22-25 will be pending in the instant application.

Objection to the Specification

In the February 25, 2008 Final Office Action the Examiner objected to the specification based on the Examiner's belief that figures were not submitted by applicant at the time the instant application was filed. Without conceding the correctness of the Examiner's belief, applicant concurrently submits herewith, copies of Figures 1-8. Accordingly, applicant respectfully submits that this objection is now moot.

Claim Objections

In the February 25, 2008 Final Office Action the Examiner objected to applicant's use of the acronym "PRA". Without conceding the correctness of the Examiner's objection, applicant has hereinabove amended the claims to replace "PRA" with the phrase "plasma renin activity" in each of the pending claims. Accordingly, applicant respectfully submits that this objection is now moot.

Rejection of Claims Under 35 U.S.C. § 103(a)

In the February 25, 2008 Final Office Action, the Examiner maintained the rejection of the claims under 35 U.S.C. § 103(a), again applying a 1978 reference by F. Gilbert McMahon ("McMahon"). The Examiner also maintained the rejection of the claims under 35

U.S.C. § 103(a), again combining McMahon with a 1998 article by John H. Laragh ("Laragh").

Applicant respectfully traverses these rejections.

Claims 22 and 23 are the only currently pending independent claims and recite, respectively:

> A method of treating a hypertensive subject having a normal to above normal plasma renin activity level comprising:
>
> A. administering to the subject or instructing the subject to take a low dose of an R drug;
>
> B. after step A, measuring the subject's BP and if the subject's BP is not controlled, administering to the subject or instructing the subject to take an increased dose of the R drug;
>
> C. after step B, measuring the subject's BP and if the subject's BP is not controlled, administering to the subject or instructing the subject to take, instead of the R drug, a low dose of a V drug; and
>
> D. after step C, measuring the subject's BP and if the subject's BP is not controlled, administering to the subject or instructing the subject to take an increased dose of the V drug,
>
> wherein said method does not include a washout period before step A.
>
> * * *
>
> A method of treating a hypertensive subject having a normal to below normal plasma renin activity level comprising:
>
> A. administering to the subject or instructing the subject to take a low dose of an V drug;
>
> B. after step A, measuring the subject's BP and if the subject's BP is not controlled, administering to the subject or instructing the subject to take an increased dose of the V drug;

C. after step B, measuring the subject's BP and if the subject's BP is not controlled, administering to the subject or instructing the subject to take, instead of the V drug, a low dose of a R drug; and

D. after step C, measuring the subject's BP and if the subject's BP is not controlled, administering to the subject or instructing the subject to take an increased dose of the R drug,

wherein said method does not include a washout period before step A.

Applicant submits that the cited references taken together or alone, do not disclose, teach or suggest applicant's presently claimed invention which is directed, *inter alia*, to utilizing plasma renin activity measurements to guide a specific course of treatment for hypertension, wherein such course of treatment does not require use of a washout period.

The McMahon Reference

Applicant first points out that McMahon is a 1978 reference which discusses the state of the art in that timeframe. Applicant's presently claimed invention is an important and significant advance over the 1970's era understanding of hypertension and reflects in part the knowledge and experience gained by the inventor, Dr. John H. Laragh, over the nearly quarter century between McMahon's publication date and the filing date of the instant application.

Applicant further points out that McMahon (1) does not in any way disclose, teach or suggest the presently claimed invention and (2) affirmatively teaches away from the presently claimed invention in at least the following four important respects. First, McMahon states that a washout period of at least two weeks is needed to obtain any useful information about PRA levels. Second, McMahon discusses several other perceived drawbacks in the use of PRA levels to guide a course of treatment such as a lack of accurate assays, collection of 24-hour

urine quantitatively, and the cost of such tests. Third, given these perceived drawbacks, McMahon argues that the Joint National Committee guidelines should be followed whereby hypertensive patients should be treated initially with a diuretic rather than directing a course of treatment based on PRA levels. Fourth, McMahon states that high renin essential hypertension would likely require a second or even a third drug in contrast to the monotherapy treatment achievable in a large majority of subjects utilizing the claimed methods.

McMahon Does Not Disclose, Teach or Suggest the Presently Claimed Invention

Applicant first points out that McMahon does not in any way disclose, teach or suggest the presently pending claims. The presently pending claims relate to specific treatment methods about which McMahon is completely silent.

For example, pending independent claim 22 relates to a method wherein subjects having a normal to above normal plasma renin activity level (1) start by taking a low dose R drug; (2) then take a higher dose R drug if BP is not controlled; (3) then switch to a V drug if BP is still not controlled; and (4) then take a higher dose of a V drug if BP is still not controlled. McMahon is silent about this method. Moreover, the method according to claim 22 occurs without need of a washout period, much less an "at least two week" washout period considered essential by McMahon.

Likewise, pending independent claim 23 relates to a method wherein subjects having a normal to below normal plasma renin activity level (1) start by taking a low dose V drug; (2) then take a higher dose V drug if BP is not controlled; (3) then switch to an R drug if BP is still not controlled; and (4) then take a higher dose of an R drug if BP is still not controlled. McMahon is silent about this method. Moreover, the method according to claim 23 occurs without need of a washout period, much less an "at least two week" washout period considered

essential by McMahon.

Accordingly, for this reason alone McMahon does not render obvious the presently pending claims.

McMahon Teaches Away from the Presently Claimed Invention

In addition, McMahon also teaches away from the claimed invention in at least four important respects.

1. McMahon Stresses Importance of Long Washout Period

McMahon stresses the importance of a long washout period by stating that "[p]atients must be taken off all antihypertensive drugs for at least two weeks because these drugs greatly effect [*sic*] the PRA levels." (McMahon, p. 3, emphasis supplied) Nowhere does McMahon suggest that this washout period can be avoided or that pre-washout plasma renin activity levels could provide any useful information to direct a course of treatment, much less the specific course of treatment recited in the pending claims. In sharp contrast, the presently claimed invention makes clear that a washout period is unnecessary. Indeed, ambulatory subjects can immediately have their PRA levels measured and begin on the appropriate medication.

2. McMahon Emphasizes Other Perceived Drawbacks

Second, McMahon discusses several other perceived drawbacks in the use of PRA levels. McMahon states:

> Is is necessary for good therapy to have classified hypertensive patients as to their renin levels? This is not a resolved issue. If these assays were uniformly accurate, and if 23 million hypertensives could collect a 24-hr urine quantitatively while being off medication for at least two weeks, and if several hundred million dollars were available to pay for these tests, one might accurately categorize a patient as having 'low-, normal' or high-

renin hypertension...

(McMahon, p. 3-4, emphasis supplied)

Thus, McMahon teaches that the barriers to using PRA levels as a guide to treatment are insurmountable from a practical standpoint. And as stated before, McMahon is completely silent as to the specific course of treatment recited in the presently pending claims. Indeed, a fair reading of McMahon reveals a degree of distain for those who might advocate the use of PRA levels to direct any type of treatment for hypertension. Accordingly, McMahon teaches away from the claimed invention in this respect as well.

3. McMahon Urges Readers to Follow Joint National Committee Guidelines

Third, given the perceived drawbacks described immediately above, McMahon argues that the Joint National Committee guidelines should be followed whereby hypertensive patients should be treated initially with a diuretic. (See McMahon, p. 4) This is in sharp contrast to the presently claimed invention whereby a specific course of treatment is based on initial PRA levels. Thus, McMahon teaches away form the claimed invention in this additional respect.

4. McMahon Teaches Use of Multiple Drugs for Many Patients

McMahon also teaches away from the present invention by stating that high renin essential hypertension would likely require a second or even a third drug. For example, as shown in McMahon's Table 1, if there is an insufficient response to the Step 1 drug, a drug from Step 2 should be added. McMahon further states that "[w]hen a patient fails on one Step 2 drug, another Step 2 drug should ordinarily be tried before proceeding to Step 3." Step 2 drugs include V drugs (e.g., prazosin) AND R drugs (e.g., clonidine) (See McMahon p. 5.) Since McMahon teaches that a Step 2 drug should be added to a Step 1 drug, the reference clearly teaches away from the presently claimed invention which does not direct the use of additional drugs for

treating hypertension, especially where both R and V drugs are administered at the same time. In sharp contrast, the claimed invention unexpectedly allows for monotherapy treatment in a large majority of patients.

Accordingly, since McMahon teaches away from the presently claimed invention in several important respects, McMahon does not render obvious the presently claimed invention.

The Laragh Reference

The Examiner again rejected the claims as obvious over McMahon in view of Laragh. The Examiner took the position that Laragh discloses a threshold level of 0.65 ng/ml/hr. A careful review of Laragh, however, confirms that the reference does not cure the deficiencies of McMahon described above.

More specifically, Laragh does not disclose, teach or suggest a course of treatment based on an initial plasma renin activity measurement, followed by administration of a V or R drug based on that plasma renin activity measurement, followed by upward titration of the V or R drug if hypertension persists, followed by a switch from V to R or R to V (as the case may be) if hypertension still persists, followed by upward titration of the recently introduced V or R drug if hypertension continues to persist, all of the above occurring without use of a washout period.

For the reasons given above, applicant maintains that McMahon and Laragh, taken together or alone, do not disclose, teach or suggest the presently claimed invention. Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 103(a).

Conclusion

In view of the foregoing, applicant respectfully requests that the Examiner reconsider and withdraw the rejections raised in the February 25, 2008 Final Office Action and allow the presently pending claims, namely claims 22-25.

No fee other than the fee for a Three-Month Extension of Time is believed to be necessary in connection with the filing of this Communication. If any additional fees are deemed necessary by the Examiner, applicant hereby authorizes such fee to be charged to Deposit Account No. 50-0540.

If a telephone interview would be of assistance in advancing prosecution of this application, applicant's undersigned attorney encourages the Examiner to telephone him at the number provided below.

Respectfully submitted,

Dated: August 22, 2008

/Robert E. Alderson/

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